REMARKS

Claims 1, 3, 6, and 20-23 have been amended. Claims 24-25 were previously cancelled. Claims 1-23 are now pending in this application. Support for the amendments is found in the existing claims and the specification as discussed below. Accordingly, the amendments do not constitute the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

Abstract

An Abstract on a separate sheet is attached.

Cross-reference to related applications.

With the preliminary amendment of January 7, 2005, the specification was amended to include a first paragraph reciting the PCT application and the foreign priority application. With this amendment, this insertion has been further modified to include a header "Cross-reference to related applications." There are no other related applications.

35 U.S.C. § 101

Claims 1, 3, and 6 are rejected under 35 U.S.C. § 101 because the conversion to "a metabolite" as specified in claims 1, 3, and 6 requires that the claim include ownership of the human cell also specified therein.

Without acquiescing to the Examiner's position, Applicants have amended claims 1, 3, and 6 to delete the term "metabolites". Accordingly, it is respectfully submitted that this ground of rejection may be withdrawn.

In view of Applicants' amendment, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph – written description

Claims 1-23 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time that the application was filed.

The Office Action states that the specification fails to provide sufficient information as to how the compounds are made, how they have been isolated and how they have been identified. However, as explained below, the present application does contain sufficient information on how to make, isolate or identify the compounds of the invention.

First, isolation of naturally occurring simmondsin has been extensively disclosed in the literature; see e.g. WO 94/25035, which is cited in the application.

Furthermore, the present specification provides a clear and complete explanation on how the compounds of the invention can be isolated from jojoba plant and identified. In reference to paragraphs [0024] to [0028] and examples 1, 2 and 3, and FIG. 1 of the published US application, it is explained how compounds of the invention can be isolated from jojoba and identified. (Note that paragraphs [0024] to [0028] correspond to the specification as filed at page 4, lines 1 to 31).

Briefly, first refined, de-oiled jojoba flour is prepared from jojoba seeds, as described in detail in example 1 and [0027] of the published application (specification as filed at page 35, lines 1-8 and page 4, lines 15-25).

A polar extract is then prepared from the refined, de-oiled jojoba flour as explained in detail in example 2 and [0027] of the published application (specification as filed at page 35, lines 10-21 and page 4, lines 15-25), by treating the flour with a polar solvent. Example 2 discloses reagents to be used and process conditions. The polar extract is then evaporated under vacuum to eliminate the solvent and the residue is further dried through lyophilization. As indicated the lyophilized product obtained, comprises primarily simmondsin and its derivatives naturally present in jojoba seeds.

The present specification gives sufficient guidance on how the compounds of the invention have been isolated and identified. Example 3 (specification as filed at page 35, line 23 to page 37, line 7) in reference to FIG. 1 of the application clearly indicates how different components of the present invention are identified and isolated from a polar extract of jojoba flour.

In addition, Applicants respectfully remark that the preparation of refined, de-oiled jojoba flour is well known in the art, and has been described in e.g. US patent 5,672,371 and WO

94/25035 which are both cited in the present application. Furthermore WO 94/25035 also discloses a method for preparing a polar jojoba flour extract and for isolating simmondsin and derivatives (analogues) thereof. A skilled person would thus have no difficulty to isolate and identify compounds according to the invention from jojoba based on the disclosures made in the specification, and further in reference to known prior art methods, which are explicitly disclosed in the specification.

Furthermore, it is noted that the compounds of the present invention can also be synthesized chemically using conventional prior art methods. Synthesis of simmondsins and derivatives thereof is not difficult and synthesis of simmondsin derivatives can readily be carried out by a person skilled in the art.

In conclusion, it is submitted that the present specification contains sufficient information about isolation and preparation of compounds according to the invention. In addition, for the isolation and synthesis of the compounds according to the invention, well-known techniques can be applied, that have been described in the prior art (see e.g. WO 94/25035 and/or US 5,672,371) which are notably referred to in the specification.

In view of Applicants' arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Claim objections

Claims 21-23 are objected to for the term "Pharmaceutical composition."

In response, claims 21-23 have been amended to "The pharmaceutical composition" as suggested by the Examiner. Withdrawal of the objection to the claims is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-23 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner asserts that claims 1, 3, and 6 are indefinite because the terms "stereoisomeric forms, racemic forms, metabolites, esters" have been incompletely defined.

Applicants first point out that this issue is moot with respect to "metabolites" as this term has been deleted in response to the rejection under 35 U.S.C. § 101.

With regard to the clarity issues raised for the terms stereoisomeric forms, racemic forms, and esters in claims 1, 3, 6 it is noted that the present specification clearly indicates the meaning of these terms and the chemical entities that correspond to these terms. Formula I of the present application presents an isomeric form of the compounds of the invention. In view of this representation in combination with the clear definitions for stereoisomeric forms and ester given in [0035] to [0039] of the published application (specification as filed at page 6, line 5 to page 7, line 13), a skilled person would know what is meant by these terms and would know to which isomers they relate. In addition chemical identification of the esters is clearly indicated in [0041] to [0043] of the published application (specification as filed at page 7, line 19 to page 8, line 2) and particular examples thereof are enumerated in the application (see [0041] and [0043] of the published application; specification as filed at page 7, line 19 to page 8, line 2).

Regarding claim 20, this claim has been amended as suggested by the Examiner.

In view of Applicants' amendments and arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 102(b)

Claims 1-23 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Flo, et al.

Flo, et al. teach that simmondsin contained in jojoba meal has an anorexic effect. The Office Action asserts that the anti-angiogenic effect of simmondsin is "inherent to the administration of consumption of jojoba flour and the chemical contents thereof" (Office Action, pages 4-5, bridging sentence).

The Examiner's position is that in administering simmondsin to reduce food intake as taught by Flo, et al, one would also be inhibiting angiogenesis. However, present claim 1 is directed to "A method of inhibiting angiogenesis in humans and animals which comprises administering a therapeutically effective amount of a simmondsin...to the human or animal in need thereof." In the present case, the term "in need thereof" gives meaning and life to the preamble that the claim is directed to inhibition of angiogenesis. Independent claims 6 and 18 also include this limitation.

As discussed in M.P.E.P. 2111.02, "If the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the claim preamble is "necessary to give life, meaning, and vitality' to the claim, then the claim preamble should be construed as if in the

balance of the claim" The M.P.E.P. cites *Jansen. v. Rexall Sundown, Inc.* 342 F 3d 1329, 1333, 68 USPQ2d 1154,1158 (Fed. Cir. 2003) (hereafter JANSEN). The claims in JANSEN were directed to "a method of treating or preventing pernicious anemia in humans by administering a certain vitamin preparation to "a human in need thereof," the court held that the claims' recitation of a patient or a human "in need" gives life and meaning to the preambles' statement of purpose" (See M.P.E.P. 2111.02 and Attachment A). Accordingly, the claims in JANSEN have a similar construction to claims 1, 6, and 18 of the present application.

In the present case, the phrase "to the human or animal in need thereof." gives life and meaning to the phrase "A method of inhibiting angiogenesis in humans and animals" and must be considered in determining patentability.

Flo, et al. do not teach a method of inhibiting angiogenesis in humans and animals by administration of "a simmondsin, stereoisomeric forms, racemic mixtures, esters or salts thereof to the human or animal in need thereof". The disclosure of Flo et al. is directed to anorexic properties of certain simmondsin derivatives which are distinct from any anti-angiogenic properties of simmondsins.

Anorexic properties cannot be compared to and are not correlated with angiogenesis inhibiting effects. Flo et al. do not provide any scientific or experimental indication or even any suggest that angiogenesis inhibiting effects could be correlated to and/or responsible for anorexic properties. Flo et al. do not refer to angiogenesis inhibition since they have only focused on anorexic properties of simmondsin.

Moreover, some simmondsins that do not have anorexic effect according to Flo et al. (i.e. 4-desmethylsimmondsin and 4,5-didesmethylsimmondsin) do have significant angiogenesis-inhibiting properties (see for instance example 5 of the present application). Clearly, the property of inhibiting food intake and anorexic effects is separate from the angiogenesis-inhibiting effects of simmondsins. Clearly, the angiogenesis inhibiting effects are not responsible for anorexic effects, and there is no support for any correlation between angiogenesis-inhibiting effects and anorexic effects.

More in particular, Flo et al. provide a study of possible anorexic effects of simmondsin derivatives. Three analogues of simmondsin were tested: simmondsin-2'-trans ferulate; 4-desmethylsimmondsin, and 4,5-didesmethylsimmondsin.

Flo et al. demonstrate that not all simmondsins have appetite-inhibiting effects. Of the four simmondsin compounds tested, Flo, et al. only demonstrate that two simmondsin compounds, simmondsin (i.e. 4,5-dimethylsimmondsin) and its ferulate (simmondsin-2'-trans ferulate) show appetite-suppressing effects. See page 1910, left column, 2nd paragraph on line 3-4 and Abstract of Flo et al. compare to paragraph [0093] and table 1 of the published application (application as filed at page 15, lines 17-19 and page 15, bottom of page).

Flo et al. explicitly state that appetite-inhibiting effects could not be demonstrated for 4-desmethylsimmondsin and 4,5-didesmethylsimmondsin (see abstract and page 1911, right column, line 9-10, page 1912, left column, 3rd paragraph). In contrast, the present specification demonstrates that 4-desmethylsimmondsin and 4,5-didesmethylsimmondsin (which have no appetite-inhibiting effects) do have angiogenesis-inhibiting effects.

In example *5.1* of the present specification, cell proliferation was measured by ^{3}H-thymidine incorporation. Figure 6 illustrates inhibition of VEGF-α-induced HUVEC proliferation by simmondsin derivatives, including 4-desmethylsimmondsin (sample B3) and 4,5-didesmethylsimmondsin (sample B5). This example provides evidence for the anti-angiogenic effect of these two simmondsin derivatives. These two simmondsin derivatives are thus able to inhibit VEGF-induced human endothelial cell proliferation (although unable to suppress appetite as shown by the cited reference, Flo, et al).

In example *5.3* of the present invention an in vitro angiogenesis assay was performed. FIG. 8B of this example shows the effect of simmondsin derivatives on *in vitro* tube formation in 3-D fibrin matrices by hMVEC. The results of this experiment show that simmondsin derivatives are able to inhibit VEGF-induced in vitro tube formation by human microvascular endothelial cells in 3-dimensional fibrin matrices. It is further highlighted that the highest biological activity was seen with desmethylsimmondsin, didesmethylsimmondsin and their respective ferulates. Accordingly, the anti-angiogenic properties of simmondsins are separate from the appetite inhibiting effects demonstrated by some of these simmondsin compounds by Flo, et al.

Furthermore, when using non-purified simmondsin derivatives, i.e. when using a polar extract from jojoba flour angiogenesis inhibiting effects can be demonstrated, see e.g. effects sample A1 (total polar jojoba extract) in FIG. 8A; FIG. 8B; FIG. 9C.

Applicants would like to emphasize that Flo et al does not teach a method for inhibiting angiogenesis or for treating a human or animal having an angiogenesis-related disease. Anorexia is not an angiogenesis-related disease. The Examiner's position seems to be that in administering a simmondsin to reduce food intake, inhibition of angiogenesis would also occur. However, the claims specify that the administration of a simmondsin is to a human or animal "in need thereof". Flo, et al. fail to recognize any human or animal in need of an anti-angiogenic treatment. For example in JANSEN cited above, while the court recognized that some of Rexall's customers might have knowingly taken the Rexall product to treat or prevent macrocytic-megaloblastic anemia, this was no more than a "theoretical possibility" or "metaphysical doubt" (see highlighted section on second to last page of Attachment A). In the case of the rats used in the study of Flo, et al., it is even more remote that any of the test animals would have been in need of an anti-angiogenic treatment as there is no evidence that any of the animals had an angiogenic-related disease or condition (such as disclosed in the present application; see paragraphs 0124-0133 which correspond to the application as filed at page 24, line19 to page 27, line 8). Accordingly, Flo, et al. do not teach all of the claim limitations.

In view of Applicants' arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Rejection under 35 U.S.C. § 102(b)

Claims 1-23 are rejected under 35 U.S.C. § 102 (a) as being anticipated by Van der Eycken.

Applicants' refer to the telephone conversation between Dr. Crane and Dan Altman which is summarized herein. During the telephone conversation, it was agreed that Van der Eycken (EP 1616874A1) is not prior art to the present application. Accordingly, withdrawal of the above ground of rejection is respectfully requested.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this

application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 9 Nov. 2007

By: Daniel Altman

Daniel E. Altman
Registration No. 34,115
Attorney of Record
Customer No. 20,995
(949) 721-2875

4495840
110507

ATTACHMENT A

United States Court of Appeals for the Federal Circuit

03-1069

CHRISTIAN J. JANSEN, JR.,

Plaintiff-Appellant,

v.

REXALL SUNDOWN, INC.,

Defendant-Appellee.

John C. McNett, Woodard, Emhardt, Naughton, Moriarty & McNett, of Indianapolis, Indiana, argued for plaintiff-appellant. With him on the brief was Steve E. Zlatos.

Gary H. Levin, Woodcock Washburn LLP, of Philadelphia, Pennsylvania, argued for defendant-appellee. With him on the brief was Lynn B. Morreale.

Appealed from: United States District Court for the Southern District of Indiana

Judge John Daniel Tinder

United States Court of Appeals for the Federal Circuit

03-1069

CHRISTIAN J. JANSEN, JR.,

Plaintiff-Appellant,

v.

REXALL SUNDOWN, INC.,

Defendant-Appellee.

DECIDED: September 8, 2003

Before LOURIE, RADER, and SCHALL, Circuit Judges.

LOURIE, Circuit Judge.

Christian J. Jansen, Jr., appeals from the final decision of the United States District Court for the Southern District of Indiana granting summary judgment that Rexall Sundown, Inc. has not infringed Jansen's U.S. Patent 4,945,083. Jansen v. Rexall Sundown, Inc., No. IP 00-1495-C-T/G (S.D. Ind. Sept. 25, 2002). Because the court correctly construed the patent claims and correctly found no genuine issues of material fact on the question of infringement, we affirm.

BACKGROUND

Jansen is the sole inventor and owner of the '083 patent, which is directed to methods of "treating or preventing macrocytic-megaloblastic anemia" by administering a combination of folic acid and vitamin B_{12} "to a human in need thereof." '083 patent, col. 6, ll. 20-24, ll. 37-41. According to the patent, deficiencies of either folic acid or vitamin B_{12} can cause

macrocytic-megaloblastic anemia, also referred to as pernicious anemia, while a deficiency of vitamin B_{12} can also cause neurological problems. Id. at col. 4, ll. 13-25. When folic acid alone is utilized to treat macrocytic-megaloblastic anemia, the folic acid may mask a vitamin B_{12} deficiency. Id.; see also id. at col. 3, l. 65 – col. 4, l. 5. An objective of Jansen's invention is to administer both supplements together to avoid the masking problem. Id. at col. 4, ll. 25-48. The independent claims read as follows:

> 1. A method of treating or preventing macrocytic-megaloblastic anemia in humans which anemia is caused by either folic acid deficiency or by vitamin B_{12} deficiency which comprises administering a daily oral dosage of a vitamin preparation to a human in need thereof comprising at least about 0.5 mg. of vitamin B_{12} and at least about 0.5 mg. of folic acid.
>
> 4. A method of treating or preventing macrocytic-magaloblastic [sic] anemia in humans which anemia is caused by either folic acid deficiency or by vitamin B_{12} deficiency which comprises orally administering combined vitamin B_{12} and folic acid to a human in need thereof in sufficient amounts to achieve an oral administration of at least about 0.5 mg. of vitamin B_{12} and at least about 0.5 mg. of folic acid within one day.

Id. at col. 6, ll. 20-24, ll. 37-41 (emphases added).

The '083 patent is a seventh-generation continuation of a patent application filed in 1970. Every member of the '083 patent's lineage was abandoned in favor of the succeeding application until the '083 patent issued in 1990. Jansen's first application claimed the method as follows:

> A method of treating or preventing anemia in humans which comprises administering a daily oral dosage of a vitamin preparation containing at least .5 mg. of vitamin B_{12} and at least .5 mg. of folic acid, whereby anemia can safely be treated orally without determining whether it is caused by folic acid deficiency or by vitamin B_{12} deficiency.

In re Jansen, 187 USPQ 743, 744 (CCPA 1975). That original claim, while specifying approximately the same amounts of folic acid and vitamin B_{12}, does not specify the type of anemia being treated and says nothing about any need on the part of the human subject. The U.S. Patent and Trademark Office ("PTO") found that claim, as well as claims directed to the

composition of matter, to be obvious in light of prior art that taught administration of folic acid alone in the claimed range, vitamin B_{12} alone in the claimed range, and combinations of the two in smaller doses than claimed. The PTO found unpersuasive Jansen's argument that administration of both components in the higher, claimed doses was an unexpected solution to the masking problem, and the Court of Customs and Patent Appeals affirmed the PTO's rejections. Id. at 746. In his next five applications, Jansen persistently attempted to gain allowance of his claims in slightly different form, yet the PTO consistently rejected his attempts. In the prosecution of his seventh application, Jansen repeated his masking-avoidance argument and submitted an article that asserted that the medical community had come to realize the effectiveness of folic acid-vitamin B_{12} combination therapy to treat pernicious anemia only after Jansen's invention date. See William H. Crosby, Improvisation Revisited — Oral Cyanocobalamin Without Intrinsic Factor for Pernicious Anemia, 140 Arch. Intern. Med. 1582 (1980). The examiner agreed but noted that the claims, being directed to unspecified anemia, were not commensurate in scope with Jansen's showing of unexpected results. Jansen thereafter agreed to cancel his composition of matter claims and to narrow his method claims by requiring a specific type of anemia, viz., macrocytic-megaloblastic anemia, rather than anemia generally, and by adding to the claims the phrase "to a human in need thereof." The PTO then issued the '083 patent to Jansen.

Rexall markets to the general public an over-the-counter dietary supplement presently known as Folic Acid XTRA™ that contains folic acid and vitamin B_{12} within the claimed ranges. The Rexall product is labeled and advertised for maintenance of proper blood homocysteine levels, but not for prevention or treatment of macrocytic-megaloblastic anemia.

Jansen sued Rexall for inducement of and contributory infringement of the '083 patent. In the district court Jansen argued that all people are "human[s] in need" of "treat[ment] or prevent[ion] of macrocytic-megaloblastic anemia," but the court, without definitively construing

the "in need" phrase, rejected that argument. Jansen, slip op. at 14. Citing, inter alia, Rapoport v. Dement, 254 F.3d 1053 (Fed. Cir. 2001), the court then construed the phrase "treating or preventing macrocytic-megaloblastic anemia" to require that, in order to infringe the patent, the human subject of the claimed method take the compound with the intent of treating or preventing macrocytic-megaloblastic anemia. Jansen, slip op. at 16. Because the court found no evidence of such intent or purpose on the part of Rexall's customers, the court granted summary judgment of noninfringement. Id. at 16-17.

Jansen timely appealed to this court, and we have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

Summary judgment is appropriate if "there is no genuine issue as to any material fact and . . . the moving party is entitled to a judgment as a matter of law." Fed. R. Civ. P. 56(c). "The evidence of the nonmovant is to be believed, and all justifiable inferences are to be drawn in his favor." Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 255 (1986). We review a district court's grant of a motion for summary judgment de novo. Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp., 149 F.3d 1309, 1315 (Fed. Cir. 1998).

A determination of patent infringement requires a two-step analysis. "First, the court determines the scope and meaning of the patent claims asserted . . . [Second,] the properly construed claims are compared to the allegedly infringing device." Cybor Corp. v. FAS Techs., Inc., 138 F.3d 1448, 1454 (Fed. Cir. 1998) (en banc) (citations omitted). Step one, claim construction, is an issue of law, Markman v. Westview Instruments, Inc., 52 F.3d 967, 970-71 (Fed. Cir. 1995) (en banc), aff'd, 517 U.S. 370 (1996), that we review de novo, Cybor, 138 F.3d at 1456. Step two, comparison of the claim to the accused device, requires a determination that every claim limitation or its equivalent is found in the accused device. Warner-Jenkinson Co. v. Hilton Davis Chem. Co., 520 U.S. 17, 29 (1997). Those

determinations are questions of fact. Bai v. L & L Wings, Inc., 160 F.3d 1350, 1353 (Fed. Cir. 1998).

On appeal, Jansen first argues that the court improperly construed the claims. More specifically, he contends that the court's construction improperly added to the claims an intent element, which is contrary to law as well as contrary to the ordinary meaning of the claim language, which does not suggest that the infringer's state of mind is relevant. Nor does the '083 patent's prosecution history, according to Jansen, suggest that the infringer's state of mind is relevant. He also argues that Rapoport does not support the court's view that a direct infringer must purposefully perform the claimed method, and that in any event Rapoport is distinguishable because that case, unlike this case, did not involve a claim to a method of prevention of a disease. According to Jansen, the phrase "a human in need thereof" encompasses a person who does not know that his or her serum levels of folic acid and vitamin B_{12} are adequate. Jansen secondly argues that he presented sufficient evidence of infringement to avoid summary judgment. According to Jansen, Rexall's formulation and labeling are circumstantial evidence of direct infringement by Rexall's customers.

Rexall responds that the court's claim construction does not add an intent element to the claims except as required by the particular language of the claims themselves. Rexall also contends that, just as in Rapoport, the claims in the '083 patent should be interpreted to require that the target group ("human[s] in need thereof") practice the method for the stated purpose ("treating or preventing macrocytic-megaloblastic anemia"), especially where, as here, the prosecution history reveals that both limitations were added for patentability. According to Rexall, a "human in need thereof" is someone either suffering from macrocytic-megaloblastic anemia or at a recognized risk, such as by medical diagnosis, of developing that condition. Rexall also responds that there is no evidence that it markets its product to the target group for the claimed purpose; on the contrary, it contends that it markets its product

only for regulation of blood homocysteine levels. Rexall further contends that, even if there were some evidence of direct infringement by its customers, it is not liable for indirect infringement, for it has not intended to cause infringement and there are substantial noninfringing uses of its product, thereby negating inducement of and contributory infringement.

We begin our claim construction, as always, with the ordinary meaning of the claim language. Rexnord Corp. v. Laitram Corp., 274 F.3d 1336, 1341 (Fed. Cir. 2001). That language requires that the method be performed on "a human in need thereof" and that the method be used "for treating or preventing macrocytic-megaloblastic anemia." The parties do not dispute what "macrocytic-megaloblastic anemia" means; instead, they dispute how the "treating or preventing" phrase and the "to a human in need thereof" phrase should be read. The issue reduces to whether such a human must know that he is in need of either treatment or prevention of that condition.

A similar issue arose in Rapoport, an interference proceeding before the PTO's Board of Patent Appeals and Interferences. The count in that case read as follows:

> A method for treatment of sleep apneas comprising administration of a therapeutically effective amount of a Formula I azapirone compound or a pharmaceutically effective acid addition salt thereof to a patient in need of such treatment . . . .

254 F.3d at 1056 (emphases added). On appeal we gave weight to the ordinary meaning of the preamble phrase "for treatment of sleep apneas," interpreting it to refer to sleep apnea, per se, not just "symptoms associated with sleep apnea." Id. at 1059. Rapoport argued that the count was unpatentable on the ground that a prior art reference disclosed that a form of the compound recited in the claim could be administered, not for treatment of sleep apnea itself, but for treatment of anxiety and breathing difficulty, a symptom of apnea. Id. at 1061. We rejected that argument, stating, "There is no disclosure in the [prior art reference that the

compound] is administered to patients suffering from sleep apnea with the intent to cure the underlying condition." Id. (emphasis added). Thus, the claim was interpreted to require that the method be practiced with the intent to achieve the objective stated in the preamble.

Just as in Rapoport, it is natural to interpret the nearly parallel language in the '083 patent claims in the same way. In both Rapoport and this case, the claim preamble sets forth the objective of the method, and the body of the claim directs that the method be performed on someone "in need." In both cases, the claims' recitation of a patient or a human "in need" gives life and meaning to the preambles' statement of purpose. See Kropa v. Robie, 187 F.2d 150, 152 (CCPA 1951) (stating the rule that a preamble is treated as a limitation if it gives "life and meaning" to the claim). The preamble is therefore not merely a statement of effect that may or may not be desired or appreciated. Rather, it is a statement of the intentional purpose for which the method must be performed. We need not decide whether we would reach the same conclusion if either of the "treating or preventing" phrase or the "to a human in need thereof" phrase was not a part of the claim; together, however, they compel the claim construction arrived at by both the district court and this court.

Our conclusion as to the meaning of the claims is bolstered by an analysis of the prosecution history. The prosecution history is often useful to ascertain the meaning of the claim language. Indeed, claims are not construed in a vacuum, but rather in the context of the intrinsic evidence, viz., the other claims, the specification, and the prosecution history. See DeMarini Sports, Inc. v. Worth, Inc., 239 F.3d 1314, 1327 (Fed. Cir. 2001). In this case, the "treating or preventing macrocytic-megaloblastic anemia" phrase and the "to a human in need thereof" phrase were added to gain allowance of the claims after almost twenty years of repeatedly unsuccessful attempts to gain allowance of claims without those phrases. We must therefore give them weight, for the patentability of the claims hinged upon their presence in the claim language. See Smith v. Magic City Kennel Club, Inc., 282 U.S. 784, 790 (1931)

("The applicant[,] having limited his claim by amendment and accepted a patent, brings himself within the rules that if the claim to a combination be restricted to specified elements, all must be regarded as material, and that limitations imposed by the inventor, especially such as were introduced into an application after it had been persistently rejected, must be strictly construed against the inventor and looked upon as disclaimers."). Furthermore, because both phrases were added simultaneously to overcome the same rejection, they should be read together, meaning that the word "thereof" in the phrase "to a human in need thereof" should be construed to refer to the treatment or prevention of macrocytic-megaloblastic anemia. Finally, that "need" must be recognized and appreciated, for otherwise the added phrases do not carry the meaning that the circumstances of their addition suggest that they carry. In other words, administering the claimed vitamins in the claimed doses for some purpose other than treating or preventing macrocytic-megaloblastic anemia is not practicing the claimed method, because Jansen limited his claims to treatment or prevention of that particular condition in those who need such treatment or prevention. Thus, the '083 patent claims are properly interpreted to mean that the combination of folic acid and vitamin B_{12} must be administered to a human with a recognized need to treat or prevent macrocytic-megaloblastic anemia.

Given that claim construction, we turn to the issue whether Jansen has raised a genuine issue of material fact regarding infringement. We conclude that he has not. Jansen has asserted indirect infringement by Rexall, premised on direct infringement by Rexall's customers. See Met-Coil Sys. Corp. v. Korners Unlimited, Inc., 803 F.2d 684, 687 (Fed. Cir. 1986) ("Absent direct infringement of the patent claims, there can be neither contributory infringement nor inducement of infringement." (citations omitted)). Jansen's theory of infringement is primarily based upon his construction of the claim that those who do not affirmatively know that they do not need to take steps to prevent or treat macrocytic-megaloblastic anemia are still "in need thereof." As explained above, that claim construction

is incorrect. Jansen nonetheless asserts that he has circumstantial evidence of direct infringement by Rexall's customers under the claim construction we and the district court have adopted. Specifically, he contends that Rexall's formulation, having folic acid and vitamin B_{12} in such large quantities as his claims call for, as well as Rexall's labeling stating that "[i]t is especially important to take B_{12} along with Folic acid because Folic acid can mask a B-12 deficiency," are evidence that some customers do knowingly take the Rexall product to treat or prevent macrocytic-megaloblastic anemia.

While Jansen is correct that it is theoretically possible that some of Rexall's customers do take the Rexall product knowingly to treat or prevent macrocytic-megaloblastic anemia, and therefore directly infringe his patent, his evidence is quite weak. In fact, he has shown no more than a theoretical possibility or "metaphysical doubt," which is insufficient to create a genuine issue of material fact. See Anderson, 477 U.S. at 261 (citing Matsushita Elec. Indus. Co. v. Zenith Radio Corp., 475 U.S. 574, 586 (1986)). The district court's decision that there were no genuine issues of material fact on the question of infringement was therefore correct.

Use of an over-the-counter product like Rexall's is quite different from the use of a product pursuant to a prescription from a medical doctor. In the latter case, a prescription is evidence of a diagnosis and a knowing need to use the product for the stated purpose. Jansen does not have evidence of that in this case. Rexall's product is provided with a label stating that the product can be used for maintenance of blood homocysteine levels, and purchasers do not necessarily know that they are in need of preventing or treating macrocytic-megaloblastic anemia. Instead, Jansen has only conjecture that some purchasers of the Rexall product might meet the daim requirements. The district court therefore did not err in holding that he failed to present sufficient proof of infringement to create a genuine issue of material fact and to thereby avoid summary judgment of noninfringement.

CONCLUSION

The district court correctly construed the claims of the '083 patent and properly determined that Jansen did not present sufficient evidence to create a genuine issue of material fact relating to infringement by Rexall. Accordingly, we

AFFIRM.